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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,776	12/12/2001	Ingrid Fritsch	ARK00797234B	9735

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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 08/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/020,776	FRITSCH ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *29-31* is/are allowed.

6)☒ Claim(s) *1-28 and 32-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/14/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 15 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a flexible polymer substrate, does not reasonably provide enablement for a flexible polymer substrate that is also a silicon wafer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. A silicon wafer is not a flexible polymer.

3. Claim 44 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention. Claim 44 apparently requires the exposed surfaces of insulating layers of a cavity in an electrode structure to be modified by attachment of

chlorosilanes that contain hydroxyl moieties. The examiner has not found in the disclosure any particular chlorosilane that may be used, let alone how the chlorosilanes can be attached to the insulating layer (and subsequently the bilayer). The specification only broadly recites, "insulator material, such as SiO_2, or Si_3N_4, can be modified [to increase or decrease wetting properties] with organohalogensilanes or organotrialkoxysilanes. Hydrophilic compounds will allow polar solvents and solutions to wet the cavities" (first full paragraph on page 19 of the specification).

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 32-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a) Claim 1 recites the limitation "devices of alternating submicroelectrodes" in line 3. There is insufficient antecedent basis for this limitation in the claim;

b) Claim 1 appears to require alternating submicroelectrodes in [the] insulating layers (line 3). Submicroelectrodes will be necessarily conducive. How can the insulating layers be both insulating and conductive?

c) Claim 1: the preamble refers to device (singular), but line 3 refers to devices (plural). Also, are the devices of line 3 electrochemical sensing devices?

d) Claim 32, line 5: -- said -- should be inserted before "conductor";

e) Claim 44: the preamble indicates that the claim is directed to an electrode structure; however, no electrode is in the body of the claim;

f) Claim 44 recites the limitation "the cavity" in line 3. There is insufficient antecedent basis for this limitation in the claim; and

g) Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are those among the electrode, insulating layers and the cavity.

6. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 28 is rejected under 35 U.S.C. 102(b) as being anticipated by the English language translation of Urban et al. (WO 90/12314 A1), hereafter "Urban."

Urban teaches a microcavity device comprising

(a) a substrate (element **5** in Figures 10-15);

(b) integrated, independently addressable electrodes (elements **1**, **2**, and **3** in Figures 10-15);

(c) conducting layers connected to the electrodes (not labeled but shown in or suggested by Figures 10-15);

(d) an insulating layer separating adjacent conducting layers (element **4** in Figures 10-13);

(e) the conducting layers and the insulating layer[s] being on top of the substrate (Figures 10-13);

(f) at least one microcavity penetrating the conducing layers and the insulating layer[s], the microcavity having a depth, a diameter, and a top opening (Figures 10-13; the last full paragraph on page 15, claim 15, and the first full paragraph on page 18); and

(g) wherein the disk electrode is recessed from the main plane of an insulting layer of the substrate (Figures 10-13).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 2-11, 13-24, 26, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over the English language translation of Urban et al. (WO 90/12314 A1), hereafter "Urban," in view of Ufer (US 2003/0085124 A1), hereafter "Ufer," and Douglas et al. (US 2003/0106810 A1), hereafter "Douglas." It should be noted that although Ufer and Douglas do not have priority before Applicants' earliest priority date of April 30, 1998, the examiner has not found support for a flexible polymer substrate in a microcavity device as claimed in any of Applicants' priority documents. Thus, until demonstrated otherwise, claims 2-25 will be accorded a priority date of December 12, 2001, which is the filing date of the instant application.

Addressing claim 2, Urban teaches a microcavity device comprising

(a) a substrate (element **5** in Figures 10-15);

(b) integrated, independently addressable electrodes (elements **1**, **2**, and **3** in Figures 10-15);

(c) conducting layers connected to the electrodes (not labeled but shown in or suggested by Figures 10-15);

(d) an insulating layer separating adjacent conducting layers (element **4** in Figures 10-13);

(e) the conducting layers and the insulating layer being on top of the substrate

(Figures 10-13); and

(f) at least one microcavity penetrating the conducing layers and the insulating layer, the microcavity having a depth, a diameter, and a top opening (Figures 10-13; the last full paragraph on page 15, claim 15, and the first full paragraph on page 18).

Urban does not mention using a flexible polymer substrate. Urban is in fact silent on possible substrate materials. However, Urban does disclose using polyimide insulator layers (last paragraph on page 17). Douglas and Ufer both teach microscale electrochemical sensor devices made of thin layers of insulating and conducting materials on a flexible substrate (the abstract; Figure 5; and paragraphs [0024] and [0026] in Douglas and the abstract; Figure 4; and paragraph [0027] and [0029] in Ufer). It would have been obvious to one with ordinary skill in the art at the time the invention was made to use a flexible substrate as taught by Douglas or Ufer in the invention of Urban because they each teach that a plurality of sensing device can then be made using continuous processing techniques (paragraph [0013] in Ufer and paragraph [0013] in Douglas), which, as taught by Douglas, "results in high volume manufacturing capability an [sic] substantial cost reductions over step and repeat processes." Also, Douglas and Ufer disclose polyimide as a possible flexible substrate material (paragraph 0021] in Douglas and paragraph [0022] in Ufer), which, as mentioned above, Urban discloses may be used for the insulating layers.

In the alternative, Ufer and Douglas are not needed to provide motivation for a flexible substrate because Urban already teaches insulating layers made from a flexible material (polyimide) and Urban teaches having the microcavity built into a catheter, which may be used

for taking measurements in body cavities (page 12, first full paragraph and page 20, first full paragraph). In a catheter embodiment it would have been obvious to one with ordinary skill in the art at the time the invention was made to have the substrate be flexible so that the catheter can be maneuvered in the patient's body with minimum discomfort and injury to the patient.

Addressing claims 3 and 17, Urban discloses having a membrane over the electrodes (second paragraph on page 11 and claim 12). From Figures 10-13 one with ordinary skill in the art at the time of the invention would have envisaged the membrane as covering the top opening. Indeed, for the embodiments in Figures 10 and 12 the membrane must cover the top opening if it is also to cover all of the electrodes.

Addressing claims 4, 5, and 18, the membrane is for "selective acquistion of certain electroactive species" (page 11, second paragraph of Urban). That is, the membrane is selectively permeable. One with ordinary skill in the art at the time of the invention would have understood that the membrane is to be permeable to analytes of interest and necessary or useful electrolytes.

Addressing claims 6, 7, 10, 19, 20, and 23 although no specific dimensions are mentioned by Urban, barring evidence to the contrary, such as unexpected results, the dimensions claimed by Applicants are just a matter of scaling the device of Urban as modified by Ufer and Douglas to best accommodate the expected sample volume because Urban clearly teaches micro and submicro scale dimensions and measuring very small analyte concentrations (second paragraph

on page 3; page 5, sixth line form the bottom to last line on page 6; claims 1 and 15; and next to last paragraphs on pages 7 and 15).

Addressing claims 8 and 21, Urban discloses band and disc electrodes (electrode **1** is a disc electrode, and electrodes **2** and **3** are band electrodes. See Figures 13 and 14, for example).

Addressing claims 9 and 22, Urban discloses at least two electrodes in the cavity (Figures 10-15).

Addressing claims 11, 13, and 24, Urban discloses providing a plurality of microcavities (Figures 14 and 15), each microcavity being a complete electrochemical cell (each microcavity comprises a measurement electrode (2), a counterelectrode (3), and a reference electrode (1)).

Addressing claims 14 and 26, that the device is a recessed disk microelectrode may be seen form Figures 10-13.

Addressing claim 16, Urban teaches a microcavity device comprising

(a) a substrate (element **5** in Figures 10-15);

(b) integrated, independently addressable electrodes (elements **1**, **2**, and **3** in Figures 10-15);

(c) conducting layers connected to the electrodes (not labeled but shown in or suggested by Figures 10-15);

(d) an insulating layer separating adjacent conducting layers (element **4** in Figures 10-13);

(e) the conducting layers and the insulating layer being on top of the substrate (Figures 10-13); and

(f) at least one microcavity penetrating the conducing layers and the insulating layer, the microcavity having a depth, a diameter, and a top opening (Figures 10-13; the last full paragraph on page 15, claim 15, and the first full paragraph on page 18);

(g) wherein the microcavity is a self-contained electrochemical cell (each microcavity comprises a measurement electrode (2), a counterelectrode (3), and a reference electrode (1). See second full paragraph on page 14); and

(h) a device for measuring electrical potential difference or current between electrodes (Urban discloses at least making potentiodynamic measurements (last line on page 6 bridging to page 7).

Urban does not mention using a flexible polymer substrate. Urban is in fact silent on possible substrate materials. However, Urban does disclose using polyimide insulator layers (last paragraph on page 17). Douglas and Ufer both teach microscale electrochemical sensor devices made of thin layers of insulating and conducting materials on a flexible substrate (the abstract; Figure 5; and paragraphs [0024] and [0026] in Douglas and the abstract; Figure 4; and paragraph [0027] and [0029] in Ufer). It would have been obvious to one with ordinary skill in

the art at the time the invention was made to use a flexible substrate as taught by Douglas or Ufer in the invention of Urban because they each teach that a plurality of sensing device can then be made using continuous processing techniques (paragraph [0013] in Ufer and paragraph [0013] in Douglas), which as taught by Douglas "results in high volume manufacturing capability an [sic] substantial cost reductions over step and repeat processes." Also, Douglas and Ufer disclose polyimide as a possible flexible substrate material (paragraph 0021] in Douglas and paragraph [0022] in Ufer), which, as mentioned above, Urban discloses may be used for the insulating layers.

In the alternative, Ufer and Douglas are not needed to provide motivation for a flexible substrate because Urban already teaches insulating layers made from a flexible material (polyimide) and Urban teaches having the microcavity built into a catheter, which may be used for taking measurements in body cavities (page 12, first full paragraph and page 20, first full paragraph). In a catheter embodiment it would have been obvious to one with ordinary skill in the art at the time the invention was made to have the substrate be flexible so that the catheter can be maneuvered in the patient's body with minimum discomfort and injury to the patient.

Addressing claims 15 and 27, Urban discloses silicon insulating layers (first full paragraph on page 18). It would have been obvious to one with ordinary skill in the art at the time the invention was made to also have the substrate made of silicon because this would simplify the manufacturing process as the substrate is essentially just another insulating layer, except, perhaps, thicker.

13. Claims 12 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Urban in view of Ufer and Douglas as applied to claims 2-11 above, and further in view of Wolf et al. (US 6,376,233 B1), hereafter "Wolf."

Urban does not mention including at least 96 well in the microcavity device, although as noted in the rejection of claim 11 Urban does does disclose a plurality of wells. Wolf discloses a microtiter plate having 96 wells with a sensor, which may be an electrode-based sensor, in each well (abstract; Figures 3 and 4; col. 2, ll. 46-53; and claim 12). Barring evidence to the contrary, such as unexpected results, to provide 96 wells as taught by Wolf in the invention of Urban as modified by Ufer and Douglas (or just Urban if the alternative motivation of claims 2 and 16 is used) is just further multiplication of parts for a multiplied effect, which is in itself obvious. It would have been obvious to one with ordinary skill in the art at the time the invention was made to proved at least 96 sensor wells as taught by Wolf in the invention of Urban as modified by Ufer and Douglas (or just Urban if the alternative motivation of claims 2 and 16 is used) so that many samples can be simultaneously and independently analyzed.

Allowable Subject Matter

14. Claims 29-31 are allowed.

15. Claims 1 and 32-43 would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

16. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 1: the nonobvious limitation in the combination of limitations is the requirement of analyte-selective organic materials suspended over a cavity penetrating alternating submicroelectrode layers and insulating layers.

Matsuo et al. (JP 04-215052 A) discloses an electrochemical sensing device having a lipid membrane suspended over a cavity comprising an electrode and an insulating layer (abstract and Figures 1 and 3). However, Matsuo et al. does not disclose alternating submicroelectrode layers and insulating layers in the cavity. As seen in Figure 2 the reference/counter electrode is outside of the cavity and suspended in the bulk solution. It would not have been obvious to provide the reference electrode also in the cavity since in order to determine the concentration of chemical material in the solution Matsuo et al. measures the film potential generated on both sides of the film (abstract), that is, across the membrane. Also, the membrane in Matsuo et al. does not have analyte-selective organic materials.

Fare et al. (US 5,5225,374) discloses an electrochemical sensing device having a lipid membrane comprising analyte-selective organic materials suspended over a cavity comprising an electrode and an insulating layer (abstract and Figure 4). However, Fare et al. does not disclose alternating submicroelectrode layers and insulating layers in the cavity. It would not have been obvious to provide an additional electrode in the cavity because the sensing device is based on an npn bipolar junction transistor (or pnp bipolar junction transistor in an alternative embodiment) wherein the cavity effectively functions as a p-base in the npn transistor col. 5, ln. 66 – col. 6, ln. 4).

Urban et al. (WO 90/12314 A1) discloses an electrochemical sensing device having a cavity comprising alternating submicroelectrode layers and insulating layers (abstract and Figures 11 and 13). However, although an English language translation of Urban et al. discloses a semi-permeable membrane arranged over the electrodes (second paragraph on page 11 and claim 12) for allowing certain electroactive species into the cavity, Urban et al. only discloses having the analyte-selective organic materials immobilized on the electrode arrangement (bottom paragraph on page 11 of the translation; second full paragraph on page 19; and claim 16), not suspended over the cavity;

b) Claim 29: the nonobvious limitation in the combination of limitations is the requirement of that the microelectrode comprise a polyimide layer and a silicon wafer on which a silicon dioxide film has been grown.

Urban is silent on possible materials for the substrate other than indicating that it be inert (last paragraph on page 14, for example). Urban does disclose an embodiment having one or more silicon layers. However, in this embodiment the silicon layers are insulation layers (first full paragraph on page 18). There is no mention in Urban of using a silicon layer in combination with a polyimide layer as is required by Applicants' claim 29 ((a) and (g)-(i)). In fact, Urban indirectly discloses polyimide as an alternative to silicon for use in forming insulating layers because Urban discloses that if polyimide insulating layers are used then deep microcavities may be formed (last paragraph on page 17 bridging to page 18);

c) Claims 30 and 31 depends from allowable claim 29;

d) Claim 32: the nonobvious limitation in the combination of limitations is the requirement that the microelectrode comprise polyimide insulating layers and a silicon wafer to act as a substrate.

Urban is silent on possible materials for the substrate other than indicating that it be inert (last paragraph on page 14, for example). Urban does disclose an embodiment having one or more silicon layers. However, in this embodiment the silicon layers are insulation layers (first full paragraph on page 18). There is no mention in Urban of using a silicon layer in combination with a polyimide layer as is required by Applicants' claim 29 ((a) and (g)-(i)). In fact, Urban indirectly discloses polyimide as an alternative to

silicon for use in forming insulating layers because Urban discloses that if polyimide insulating layers are used then deep microcavities may be formed (last paragraph on page 17 bridging to page 18); and

e) Claims 33-43 depend directly or indirectly from allowable claim 32.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
August 6, 2004